-- 22. (New) The fluid pharmaceutical composition of claim 1 wherein the micelles have an average diameter less than about 100 nm. --

-- 23. (New) The fluid pharmaceutical composition of claim 1 wherein the micelles have an average diameter less than about 50 nm. --

-- 24. (New) The fluid pharmaceutical composition of claim 1 wherein the micelles have an average diameter from about 3 nm to about 25 nm. --

Cancel claims 2, 3, and 6.

Remarks

The Office Action dated December 4, 2000 has been carefully considered. Claims 1, 4, 5 and 7-21 have been amended. Claims 2, 3 and 6 have been cancelled. Claims 22-24 have been added. Claims 1, 4, 5 and 7-24 are in this application.

The limitation of original claim 2 has been added to claim 1. Support for new claims 22-24 is found throughout the specification and in particular on page 27, lines 12-17.

The previously presented claims were rejected under 35 USC § 102(e) as anticipated by U.S. Patent No. 5,891,469 to Amselem. Applicant submits that this reference does not teach or suggest the invention defined by the present claims.

Amselem discloses a solid dry coprecipate compositions containing lipophilic active ingredients and tocopherol polyethyleneglycol succinate (TPGS). The solid composition is obtained by co-melting TPGS, freeze drying or spraying drying.

In contrast to the invention defined by the present claims, Amselem does not teach or suggest a fluid pharmaceutical composition comprising an aqueous dispersion of micelles. To the contrary, Amselem teaches a solid composition. Furthermore, Amselem does not disclose or suggest that an aqueous dispersion is formed of micelles having an average diameter of less than about 300 nm.

As described on page 25, line 30-page 26, line 20 of the application, the micelles of the present invention have the advantage of protecting the biological

agent for uptake by non-target tissues and having able to penetrate in small capillaries and to be taken up by the cells. There is no teaching or suggestion of the size of micelles in Amselem and the advantages achieved by a particular size of micelles. In addition, Amselem does not teach or suggest a method of treating an animal by administering a fluid pharmaceutical composition comprising an aqueous dispersion of micelles having an average diameter of less than about 300 nm. Also, Amselem does not teach or suggest a method of delivering a podophyllotoxin of etoposide and teniposide by administering a fluid pharmaceutical composition comprising an aqueous dispersion of micelles having an average diameter less than about 300 nm. Accordingly, the invention defined by the present claims is not anticipated by Amselem.

The previously presented claims were rejected under 35 USC § 103 as obvious in view of Amselen in combination with Brandely et al. Brandely et al. teach a polypeptide having human interleuken 2 (IC) activity for the treatment of cancer. However, Brandely et al. do not teach or suggest a fluid pharmaceutical composition comprising an aqueous dispersion of micelles having an average diameter less than about 300 nm. Thus, Brandely et al. do not cure the deficiencies of Amselem noted above. Further, with regard to claim 11, applicant submits that Amselem describes a weight percentage in a solid wherein in the present invention the weight percentage is determined in a liquid. Accordingly, the range of concentration of TPGS in the Amselem composition is different than the range of concentration of TPGS in the present invention. Accordingly, the invention is not obvious in view of Amselem in combination with Brandely et al. since neither reference teaches a fluid pharmaceutical composition comprising an aqueous dispersion of micelles having an average diameter less than about 300 nm, the micelles comprising a podophyllotoxin of eptoside or teniposide and a surfactant.

In view of the foregoing, Applicant submits that all pending claims are in condition for allowance and requests that all claims be allowed. The Examiner is invited to contact the undersigned should he believe that this would expedite prosecution of this application. A fee in the amount of $890 for a three-month

pharmaceutical composition comprising an aqueous dispersion of micelles having an average diameter less than about 300 nm, the micelles comprising a podophyllotoxin of eptoside or teniposide and a surfactant.

In view of the foregoing, Applicant submits that all pending claims are in condition for allowance and requests that all claims be allowed. The Examiner is invited to contact the undersigned should he believe that this would expedite prosecution of this application. A fee in the amount of $890 for a three-month extension of time is enclosed. The Commissioner is authorized to charge any deficiency or credit any overpayment to Deposit Account No. 13-2165.

Respectfully submitted,

Diane Dunn McKay
Reg. No. 34,586
Attorney for Applicants

DATE: June 7, 2001

MATHEWS, COLLINS, SHEPHERD & GOULD, P.A.
100 Thanet Circle, Suite 306
Princeton, New Jersey 08540-3662
Telephone: (609) 924-8555
Telecopier: (609) 924-3036

Clean version of replacement claims:

1. A fluid pharmaceutical composition comprising an aqueous dispersion of micelles having an average diameter less than about 300 nm, said micelles comprising:

a podophyllotoxin selected from the group consisting of etoposide and teniposide, and

a surfactant selected from the group consisting of tocoferol and tocoferol covalently linked to a water-soluble polymer.

4. The fluid pharmaceutical composition of claim 1 wherein the podophyllotoxin is etoposide.

5. The fluid pharmaceutical composition of claim 1 wherein the surfactant is tocoferol.

7. The fluid pharmaceutical composition of claim 1 wherein the water-soluble polymer is poly-oxyethylene, poly-oxyethylene-poly-oxypropylene copolymers polyacrylamides, polyglycerols, polyvinylalcohols, polyvinylpyrrolidones, polyvinylpyridine N-oxides, copolymers of vinylpyridine N-oxide and vinylpyridine, polyoxazolines, polyacroylmorpholines or derivatives thereof.

8. The fluid pharmaceutical composition of claim 1 wherein the water-soluble polymer is a polypeptide or derivative thereof.

9. The fluid pharmaceutical composition of claim 1 wherein the water-soluble polymer further comprises a second hydrophobic group in addition to tocoferol.

10. The fluid pharmaceutical composition of claim 1 wherein the surfactant is d-α-tocopheryl polyethylene glycol 1000 succinate or a derivative thereof.

11. The fluid pharmaceutical composition of claim 10 wherein the d-α-tocopheryl polyethylene glycol 1000 succinate is present at a concentration from about 0.02 wt % to about 20 wt %.

12. The fluid pharmaceutical composition of claim 10 wherein the d-α-tocopheryl polyethylene glycol 1000 succinate is present at a concentration from about 0.02 wt % to about 10 wt %.

13. The fluid pharmaceutical composition of claim 10 wherein the d-α-tocopheryl polyethylene glycol 1000 succinate is present at a concentration from about 4 wt % to about 10 wt %.

14. The fluid pharmaceutical composition of claim 1 further comprising a targeting molecule.

15. The fluid pharmaceutical composition of claim 14 wherein the targeting molecule comprises a targeting moiety and a lipophilic moiety.

16. The fluid pharmaceutical composition of claim 15 wherein the targeting moiety is an antibody, hormone, carbohydrate, drug, cytokine, or interleukin.

17. The fluid pharmaceutical composition of claim 15 wherein the targeting moiety is a peptide.

18. A method of treating an animal comprising administering to the animal a fluid pharmaceutical composition comprising an aqueous dispersion of micelles having an average diameter less than about 300 nm, said micelles comprising:

a podophyllotoxin selected from the group consisting of etoposide and teniposide, and

a surfactant selected from the group consisting of tocoferol and tocoferol covalently linked to a water-soluble polymer.

19. The method of claim 18 wherein the surfactant is TPGS or a derivative thereof.

20. A method of delivering a podophyllotoxin selected from the group consisting of etoposide and teniposide to a cell comprising administering to the cell a fluid pharmaceutical composition comprisingan aqueous dispersion of micelles having an average diameter less than about 300 nm, said micelles comprising:

a podophyllotoxin selected from the group consisting of etoposide and teniposide; and

a surfactant selected from the group consisting of tocoferol and tocoferol covalently linked to a water-soluble polymer.

21. A method of inhibiting cancer comprising administering to an animal having cancer a fluid pharmaceutical composition comprising an aqueous dispersion of micelles having an average diameter less than about 300 nm, said micelles comprising:

a podophyllotoxin selected from the group consisting of etoposide and teniposide; and

a surfactant selected from the group consisting of tocoferol and tocoferol covalently linked to a water-soluble polymer.

22. The fluid pharmaceutical composition of claim 1 wherein the micelles have an average diameter less than about 100 nm.

23. The fluid pharmaceutical composition of claim 1 wherein the micelles have an average diameter less than about 50 nm.

24. The fluid pharmaceutical composition of claim 1 wherein the micelles have an average diameter from about 3 nm to about 25 nm.